Multi-Institutional Analysis of rCBV Measurements from DSC MRI of Low-Grade Gliomas Predicts Patient Outcome Better than Histopathology

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INTRODUCTION: Histopathology remains the standard reference for determining glioma grade/tumor biology. However, histopathology is limited by sampling error, by inter- and intraobserver variability, and by the dynamic nature of gliomas, whereby tumors can de-differentiate into more aggressive phenotypes (1,2). The purpose of this study is to determine whether relative cerebral blood volume (rCBV) can predict patient outcome, specifically tumor progression and malignant transformation, in low-grade gliomas (LGGs) at multiple institutions, thus addressing the concerns associated with pathologic diagnosis.

MATERIALS AND METHODS: Sixty-nine patients were studied with dynamic susceptibility contrast-enhanced perfusion MRI (DSC MRI) at both institutions. The pathologic diagnoses were: 34 low-grade astrocytomas, 20 low-grade oligodendroglioma, 9 low-grade mixed oligo-astrocytomas, 1 ganglioglioma, and 5 with indeterminate histology. Wilcoxon tests were used to compare patients in different response categories (complete response, stable, progressive, death) with respect to baseline rCBV. Kaplan-Meier time-to-progression curves were generated. Log-rank tests were used to predict the association of CBV with survival and time to progression using both numeric values and binary indicator variables for rCBV—the latter refers to rCBV values greater or less than 1.75. Measurements of rCBV were obtained by choosing the highest regional intratumoral rCBV after excluding large intratumoral vessels.

RESULTS:
Using the data from both institutions, the rCBV for patients with no adverse event (complete response or stable disease) was 1.71 ± 0.86 (mean ± SD), whereas that of patients with an adverse event (progressive disease or death) was 2.56 ± 1.52 (p value = 0.0138). The odds ratio to assess the utility of rCBV for the detection of adverse events is 1.87 (95% confidence interval: 1.14, 3.08). Using the log-rank test, rCBV was significantly negatively associated with time to progression (p=0.0059, 0.0057 for numeric and binary representations of rCBV, respectively). Furthermore, there was no indication (p>0.4) that the association of rCBV with time to progression was different at both institutions. The median time to progression among subjects with rCBV > 1.75 was 365 days (95% confidence interval: 355 to 742 days). While the median time to progression among subjects with rCBV < 1.75 could not be estimated (since more than 50% of these subjects were progression-free at time of last observation), there is 95% confidence that the median in this cohort is at least 889 days.

Figure 1. Kaplan-Meier survival curves representing the probability of progression free survival as a function of baseline rCBV.

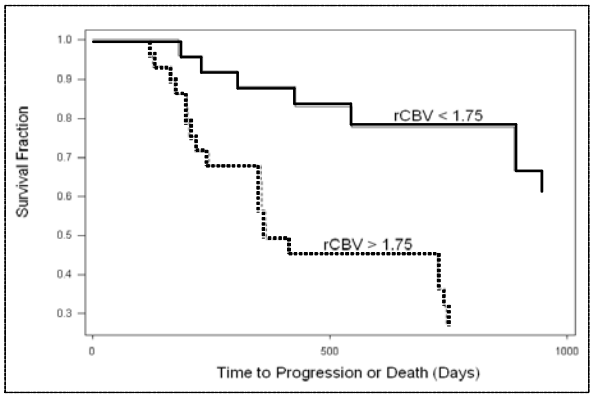

Figure 1. Kaplan-Meier survival curves for demonstrating the probability of time to progression at the most recent clinical follow up. LGGs with CBV < 1.75 had a median time to progression likely greater than 889 days (black solid curve which is far right shifted). LGGs with CBV > 1.75 had a median time to progression of 365 days (95% confidence interval: 355 to 742 days (black dashed curve which is far left shifted, p < 0.0138). The data suggests that baseline CBV may be a stronger predictor of patient outcome than the initial histopathology.

CONCLUSION: The current gold standard of histopathologic glioma grading has limitations. Partly because of this, the triage, treatment and survival statistics of low-grade gliomas remains a challenge. Patients with misclassified gliomas may not receive optimum treatment. DSC MRI has previously been shown to be effective in predicting time to progression and in differentiating between high and low grade glioma at a single institution (3,4). Our study not only suggests that cerebral blood volume measurements correlate more accurately with time to progression than initial histolopathologic grading, but also that the findings can be replicated at multiple institutions, which supports the application of rCBV as an adjunct to the pathology in predicting glioma biology.

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